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MATCHING UNDER NONINDEPENDENT VARIABLE-RATIO SCHEDULES OF DRUG REINFORCEMENT

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Response-contingent deliveries of oral pentobarbital maintained responding of 3 rhesus monkeys during daily 3-hr sessions. Deliveries of pentobarbital were arranged under nonindependent concurrent variable-ratio variable-ratio schedules. Responses to either schedule counted toward completion of both variable-ratio schedule requirements. This schedule is similar in some respects to conventional concurrent variable-interval variable-interval schedules, in which passage of time counts toward completion of the interval value on both schedules. Restricted nonindependent concurrent variable-ratio variable-ratio schedules were also studied. On that schedule, when a drug delivery was assigned to one spout, it had to be collected before responses on the opposite spout again counted toward completion of the schedule requirements. Relative reinforcer magnitude was varied by changing the drug concentration on one schedule while keeping the drug concentration constant on the other variable-ratio schedule. Under both types of concurrent variable-ratio variable-ratio schedules, the relative rate of responding corresponded to the relative drug intake. Unlike earlier studies of concurrent variable-interval variable-interval intravenous cocaine reinforcement, preference was proportionate to concentration, and exclusive preferences did not develop. The relationship between relative rate of responding and relative drug intake was well described by the generalized matching law.

Key words: generalized matching law, reinforcement magnitude, concurrent variable-ratio schedules, drug self-administration, pentobarbital, spout-contact response, rhesus monkeys

Response rate is not always a reliable indicator of the relative reinforcing effects of different drug doses. This limitation of response rate can be illustrated by studies that employ drug reinforcers. In drug self-administration studies, the functional relationship between response rate and drug dose is that of an inverted U-shaped or bitonic function (Katz, 1989). The highest dose usually maintains a lower response rate than does an intermediate dose, perhaps due to satiation (Katz, 1989) or to factors such as unconditioned or direct drug effects (Skjoldager, Winger, & Woods, 1991; Woolverton & Johanson, 1984). In contrast, when different doses are concurrently available, higher doses are preferred to lower doses (Iglauer & Woods, 1974; Johanson & Schuster, 1975).

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In one series of studies, the matching law (Herrnstein, 1970) was used to analyze behavior reinforced by intravenous cocaine under concurrent variable-interval (VI) VI schedules (Iglauer & Woods, 1974; Llewellyn, Iglauer, & Woods, 1976). Results consistent with the matching law were obtained: Relative response rates approximated relative drug intake (Iglauer & Woods, 1974). However, at high doses response rates were low. After self-injection of a high dose, there was often a long pause; the first response emitted at the end of this long pause resulted in a drug injection. Under these conditions, exclusive side preferences developed. To remedy this problem, concurrent VI VI schedules were modified so that both schedules stopped advancing until a reinforcer scheduled on one of them was collected (Llewellyn et al., 1976). As the comparison dose was increased, there was an increase in preference for the comparison dose up to the dose size just larger than the constant dose. When the comparison cocaine dose was further increased, there was no consistent increase in preference. Thus, it was not possible to obtain graded increases in responding at doses above the constant dose.

In another series of studies, two procedures were used to scale the relative reinforcing effects of different oral drug concentrations. One procedure assessed preference between concentrations of the barbiturate pentobarbital (Meisch & Lemaire, 1988, 1989), and the other assessed persistence of responding in the face of increasingly demanding response requirements (Lemaire & Meisch, 1984, 1991). Persistence increased directly with increases in concentration (Lemaire & Meisch, 1984). Preference was measured under conditions of concurrent access to two concentrations (Meisch & Lemaire, 1988; Meisch, Lemaire, & Cutrell, 1992). Concurrent fixed-ratio (FR) FR schedules or signaled concurrent differential-reinforcement-of-low-rate (DRL) DRL schedules were employed. Unfortunately, these schedules generally did not yield graded preference functions. However, when systematic comparisons of many concentration pairs were conducted under these schedules, it was possible to construct an ordinal ranking of concentrations. In these studies, the highest pentobarbital concentration was the most preferred; relative preference declined with decreases in concentration (Meisch & Lemaire, 1988, 1989). A disadvantage of this extended comparison procedure is that it is time consuming. Thus, an evaluation of drug concentrations would be advanced by a method that yields graded preferences and requires fewer comparisons.

An alternative approach is the use of concurrent variable-ratio (VR) VR schedules in which low response rates do not alter relationships between responding and reinforcer delivery. Shull and Pliskoff (1971) described concurrent VR VR schedules under which responses on either key incremented the counters for both VR schedules. Under conventional concurrent VI VI schedules, progress toward completion of the response requirement on both schedules occurs with the passage of time. Similarly, under the nonindependent concurrent VR VR schedules, responses on either side increment both VR counters. In a study of food-reinforced behavior in rats, MacDonall (1988) arranged concurrent VR VR schedules in the manner described by Shull and Pliskoff. MacDonall found that the relative rate of responding matched the relative rate of food pellet delivery.

In the present study, the concurrent schedule introduced by Shull and Pliskoff (1971) was used with rhesus monkeys to study behavior maintained by oral delivery of pentobarbital. A variant of the concurrent VR VR schedules, under which the monkey obtained similar numbers of liquid deliveries from each spout, was also examined. This schedule is a restricted nonindependent concurrent VR VR schedule and is similar to dependent concurrent VI VI schedules in that progress toward completion of the schedule requirement is terminated until the withheld reinforcer is collected. The objectives of the present study were to determine (a) if graded preference functions would develop, (b) if matching would occur, and (c) if exclusive preferences could be avoided.

METHOD

Subjects

The subjects were 3 adult male rhesus monkeys (*Macaca mulatta*) who had 5 or more years of experience with oral pentobarbital self-administration. In general, their behavior had been maintained under FR schedules, and they had been subjects in a number of prior pentobarbital self-administration studies (e.g., Macenski, Cutrell, & Meisch, 1993; Meisch & Lemaire, 1988; Meisch et al., 1992). The monkeys were maintained at a fixed percentage of their free-feeding weights through daily feeding with a measured amount of commercially available chow (Lab Diet high-protein monkey diet 5045 PMI™ Feeds) plus fresh fruit and a children's multiple vitamin pill daily. Water was available 18 hr a day, as described below. The monkeys were weighed once a month; during the study, weights ranged from 8.9 to 9.5 kg (for Monkey LA), from 8.2 to 8.6 kg (for Monkey P), and from 8.6 to 9.0 kg (for Monkey G2). These weights corresponded to 79% (Monkey LA), 78% (Monkey P), and 84% (Monkey G2) of their free-feeding weights. Access to food was restricted because such conditions increase drug-reinforced behavior (Carroll & Meisch, 1984). Also, food restriction may promote health and extend life span (Masoro, 1985). Monkeys can become obese after being housed individually in a cage with unlimited access to food (Meisch & Lemaire, 1989). The monkeys' health and appearance were good. Animal care was in accordance with the regulations of the Committee on Care and Use of Laboratory Animal Resources, Institute of Laboratory Animal Resources (1985).

Apparatus

Each subject was individually housed 24 hr a day in a stainless-steel primate cage (Lab Products), which also served as the experimental chamber. Each cage had three solid walls and one barred wall. Cage dimensions were 76 cm by 102 cm by 81 cm. A liquid-delivery apparatus panel was attached to the outside of one side wall, and spouts and stimulus lights protruded into the cage through holes cut in that wall. Attached to the back of the apparatus panel was a T-shaped bar; on each limb of this bar was fastened a stainless-steel reservoir covered with a lid. Liquids contained in each reservoir passed through polyethylene tubing to a solenoid-operated valve at the rear of one of the two brass spouts. These spouts (1.2 cm outside diameter, 0.2 cm inside diameter) protruded 2 cm into the cage, 64 cm above the floor and 15.5 cm either side of the midline. The spouts were embedded in Plexiglas disks that covered the 7-cm diameter holes in the cage wall through which they entered. At each spout, two 1.1-W lights, one located 2.5 cm on either side of the spout and visible through the Plexiglas, were aligned diagonally; these ''spout lights'' were capped with green translucent lenses. Another two 1.1-W spout lights, one located 2.5 cm on either side of the spout, were aligned on the opposite diagonal, and were capped with white translucent lenses. Thus, each spout was in the center of a square pattern of four spout lights, two green and two white. The electronic components for the drinkometer circuit were housed in an enclosure at the rear of the spout. The liquid-delivery apparatus has been described extensively elsewhere (Gieske, 1978; Henningfield & Meisch, 1976). A cluster of green light-emitting diodes (2.5 cm diameter) was located 11.5 cm directly above each brass spout. The programming of experimental events and the recording of behavior were accomplished with a DEC PDP-11 computer and SKED® software. This equipment was located in a room near the rooms containing the experimental chambers.

Procedure

Sessions. Experimental sessions were 3 hr in length (from 11:00 a.m. to 2:00 p.m.) and were conducted 7 days per week. During experimental sessions, the green stimulus lights above each spout blinked at a rate of 10 Hz. Each lip contact with a spout illuminated the green-lensed pair of spout lights for the duration of the response. That responses were made by lip contact has been verified by observers in the room housing the experimental chambers and by observers monitoring drinking by closed-circuit television. Liquid delivery was contingent upon making a number of spout contacts; the number varied from reinforcer to reinforcer (VR reinforcement schedule). The final response in the VR requirement initiated the liquid flow. For each liquid delivery, the solenoid-operated valve was activated for approximately 150 ms, allowing approximately 0.65 ml of liquid to pass through the spout and into the monkey's mouth. To minimize spillage, solenoid activation terminated if lip contact with the spout was broken before the 150-ms interval had elapsed. The reinforcer magnitude was varied by use of different drug concentrations. The side from which each of two concentrations was available alternated daily to control for possible side bias.

Under the nonindependent concurrent VR VR schedules, responses on each spout counted toward completion of both VR values (MacDonall, 1988; Shull & Pliskoff, 1971). When a drug delivery was scheduled on the opposite side from which responding was occurring, it was withheld until the monkey switched to that spout. The VR values were selected in the manner MacDonall employed. The sequences of values in all schedules were exponentially distributed according to the method of Fleshler and Hoffman (1962), with the exception that values expressed by them in seconds were used as response numbers. During the first phase of this study, the VR value was 32 for both schedules. At VR 32, 19 values were randomly picked and were used without replacement until all values had been used. Subsequently, these 19 values were again randomly selected (1, 2, 4, 6, 8, 10, 13, 18, 21, 24, 27, 31, 36, 41, 48, 56, 67, 84, and 143). The concurrent VR VR requirements selected for each monkey were the largest requirements under which response rates were high and stable.

Under the restricted nonindependent concurrent VR VR schedules, the requirements were the same as in the nonindependent concurrent VR VR schedule, with the important exception that once a liquid delivery was scheduled for one spout, responses on the opposite spout no longer counted toward completion of its VR requirement. After the earned delivery was collected, responses again counted toward completion of both VR values.

With Monkeys G2 and P, the effects of imposing a changeover ratio (COR) requirement were examined. Changeover ratios were studied to determine the range of conditions over which orderly behavior occurred. With Monkey G2, a COR of 4 was used in combination with a restricted nonindependent concurrent VR 16 VR 16 schedule, and with Monkey P a COR of 4 was studied in combination with a nonindependent concurrent VR 64 VR 64 schedule. Under this contingency, a minimum of four responses was required after switching spouts before a liquid delivery could be obtained.

Appendixes A, B, and C list for each subject the sequence of test conditions. The standard pentobarbital concentration was always 2.00 mg/ml, and the comparison concentrations were 1.00, 1.41, 2.00, 2.82, and 4.00 mg/ml. Concentrations were selected that resulted in a broad range of response rates. The dose was 0.65 ml of drug solution. The pentobarbital concentrations were presented in an ascending and a descending sequence. This counterbalanced sequence permits the detection of order effects. Each condition was in effect until six consecutive sessions of stable behavior were obtained. Stability was judged by visual inspection of whether there was an absence of upward or downward trends in numbers of responses and liquid deliveries. Appendixes A, B, and C give the total numbers of sessions in each condition.

Between sessions. A timeout, in which the drinking devices could not be operated, was in effect during the hour immediately before the session (10:00 a.m. to 11:00 a.m.). During this period, the number of water deliveries and the volume of water consumed since the last experimental session were recorded, and liquids appropriate for the sessions were placed in the monkeys' reservoirs. Some of each solution was drained through the tubing leading from the reservoir to ensure that the appropriate solution was present on the first delivery of the session. Liquid volumes were measured after flushing to obtain the exact volume in the reservoirs at each session's outset. For 1 hr immediately following the session (2:00 p.m. to 3:00 p.m.), another timeout period was in effect. During this period, numbers of liquid deliveries and volumes of liquid consumed during the session were recorded; water was placed in one of each monkey's reservoirs and flushed through the tubing to the spout. Water was then available under an FR 1 schedule from one spout from 3:00 p.m. until 4:00 p.m. The spout from which water was available between sessions alternated from day to day. A final timeout period was in effect from 4:00 p.m. to 5:00 p.m., at the beginning of which the monkeys' maintenance feeding was placed in the food hopper attached to the cage. From 5:00 p.m. to 10:00 a.m. of the next day, water was available under an FR 1 schedule from one spout. When water was available from a spout between sessions, the green stimulus lights above that spout were illuminated continuously. Each lip contact on that spout resulted in delivery of water and illumination of the white-lensed pair of spout lights for the duration of the lip contact. Responses on the spout at which water was not available were recorded but had no programmed consequences; the stimulus light over this spout was not illuminated. A 12:12 hr light/dark cycle was in effect, with lights on at 6:00 a.m. and going off at 6:00 p.m.

Drug. A 6.25 mg/ml stock solution of sodium pentobarbital was prepared weekly and stored at 3 °C for a maximum of 7 days. Drug solutions were prepared by further diluting the stock solution with tap water 2 hr before each session, which allowed the solutions to be at room temperature at the start of each session. All drug concentrations are expressed in terms of the salt.

Data analysis. The mean number of responses per second, the mean number of drug deliveries, and the mean drug intake were calculated across the last six sessions of each condition. Drug intake per hour of session was calculated by multiplying the drug concentration by the volume consumed and then dividing the product by the monkey's weight and then by 3 hr.

The generalized matching law describes the relationship between relative rates of responding and relative rates of reinforcer deliveries or reinforcer magnitudes in concurrent schedules. The generalized matching law is expressed by

$$\log(R_1/R_2) = a \log(M_1/M_2) + \log c, \quad (1)$$

where R_1 and R_2 refer to the responses made on the respective alternatives, and M_1 and M_2 are the reinforcer magnitudes or reinforcer frequencies associated with each alternative; a and c are fitted parameters. In this study, M_1 and M_2 are the amounts (in milligrams) of pentobarbital consumed from the comparison and standard solutions. The parameter a, the slope, is a measure of the sensitivity of relative response rates to relative reinforcer intakes (Baum, 1974, 1979; Davison & McCarthy, 1988). The closer a is to 1.00, the greater is the correspondence between changes in relative response rates and changes in relative drug intakes. The log c parameter is a measure of bias by factors unrelated to reinforcement rate. Deviation of log c from zero suggests control by factors other than reinforcer magnitude, such as a position preference. Equations for the best fitting straight lines were obtained using the method of least squares.

RESULTS

Time course. The overall time course of responding consisted of a high rate of responding at the beginning of the session followed by extended pauses that were punctuated by several bouts of responding in the second and third hours. These bouts were usually smaller than at the beginning of the session. This time course of pentobarbital drinking has been observed repeatedly (e.g., Lemaire & Meisch, 1984). Each bout consisted of responding at a high rate, in a pattern characteristic of performance under ratio schedules.

Generalized matching relation. The top rows of Figures 1, 2, and 3 show that for all 3 monkeys and across all experimental conditions there was a strong correspondence between the relative amounts of pentobarbital consumed and the relative number of responses maintained by the comparison solution. The a parameter, a measure of sensitivity to the reinforcer distribution, ranged from 0.96 to 1.77. The generalized matching relation accounted for a substantial proportion of the variance. The R^2 value ranged from .96 to 1.00 for six of the seven values calculated. Overmatching ($a > 1.00$) was observed under the nonindependent concurrent VR VR and the restricted nonindependent concurrent VR VR schedules. When a COR was added (top row, Figure 3), the measures of sensitivity to the reinforcer distribution were close to 1.00 (1.14 and 0.99 for Monkeys G2 and LA, respectively). At each concentration, the results of the first and second determinations were similar.

Response rate. The bottom rows of Figures 1, 2, and 3 show response rates maintained by the standard and comparison solutions; Appendixes A, B, and C give the standard errors for these mean rates. Response rates maintained by the comparison solutions increased as pentobarbital concentration increased. There was a reciprocal decrease in response rate maintained by the 2 mg/ml standard solution. For Monkey G2, the range of response rates was narrow, which perhaps was due to the relatively small VR value (16) for this monkey. Under the restricted schedules, similar numbers of deliveries of the standard and comparison solutions were obtained. In spite of this restriction, response rates differed substantially (see Appendix B).

Overall response rate and drug intake as a function of the comparison concentration. Appendixes A, B, and C show that for all monkeys and schedules, the total drug intake (milligrams of pentobarbital per kilogram of body weight per 3 hr) increased as the pentobarbital concentration of the comparison solution increased.

Under the nonindependent concurrent VR VR schedules, overall response rate decreased as the comparison concentration increased (Appendix A). In contrast, under the restriction contingency, overall response rates were relatively constant (Appendix B). The addition of the COR requirement produced no systematic change in overall rate (Appendix C). Monkey LA's overall rate differed from Monkey G2's rate in that an abrupt decrease occurred when the concentration was changed from 1.00 to 1.41 mg/ml. Subse-

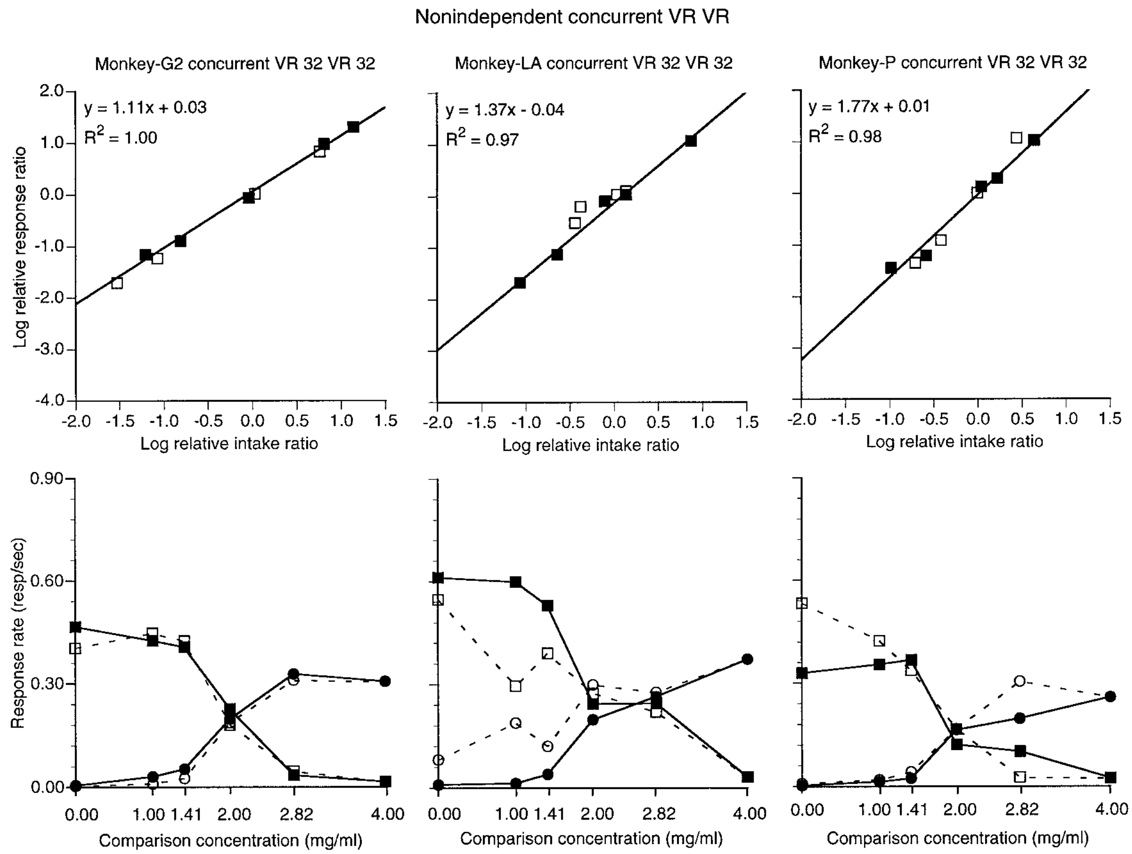

Fig. 1. Performance under the nonindependent concurrent VR VR schedules. Each point is the mean from the last six consecutive sessions of each condition. Top row: Mean response ratios in log units are plotted as a function of the mean drug-intake ratios in log units. Filled squares: ascending concentration sequence. Open squares: descending sequence. The solid line represents the least squares regression line. Bottom row: mean response rate as a function of the pentobarbital concentration of the comparison solution. Squares: standard concentration (2 mg/ml) mean. Circles: comparison solution mean. Filled symbols: ascending concentration sequence. Open symbols: descending concentration sequence. See Appendix A for the standard error of the means (*SEM*).

quently, Monkey LA's overall rate increased slightly as the comparison concentration increased.

For all monkeys, responding on the comparison spout was not maintained by delivery of the vehicle, tap water (0.00 mg/ml). For Monkey LA, responding on the standard spout was not maintained by the 1.00 mg/ml solution on the descending dose sequence under the COR 4 requirement.

DISCUSSION

Relative response rates matched relative drug intake, and this occurred under several modifications of the nonindependent concurrent VR VR schedules. In contrast, when pentobarbital concentrations were available under concurrent FR FR schedules in a previous study, matching did not occur (Meisch & Lemaire, 1988). Findings in both studies can be compared when there were similar differences between the standard and comparison concentrations. Under the concurrent FR FR schedule, less than 1% of the responses were maintained by the lower concentration (Meisch & Lemaire, 1988). The present results differ from those of that study in that the proportion of responses maintained by the comparison solution increased in graded steps as its pentobarbital concentration increased. Out of 35 comparisons of unequal concentrations in the present study, an exclusive preference (proportion of re-

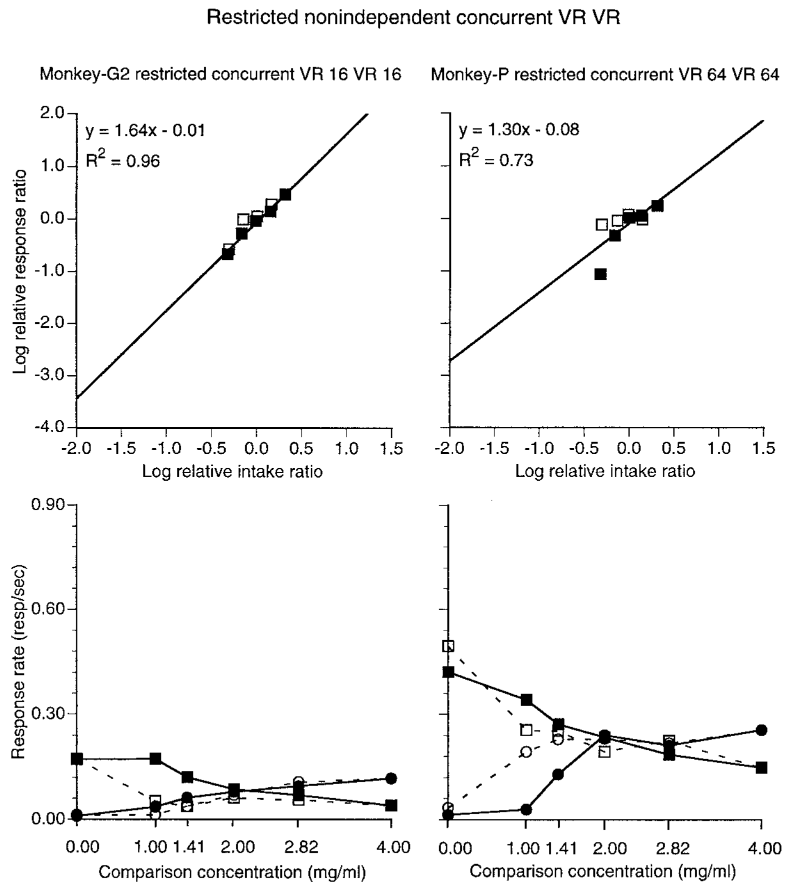

Fig. 2. Performance under the restricted nonindependent concurrent VR VR schedule. See Appendix B for the standard error of the means (*SEM*). All other details are the same as Figure 1.

sponding maintained by one concentration being greater than .99) was seen in only four comparisons; these comparisons were between drug and water, with which an exclusive preference would be the expected outcome. Our findings differ from those of Iglauer and Woods (1974), who used concurrent VI VI schedules. They observed exclusive preferences in 22 of 36 comparisons of unequal cocaine doses (Iglauer & Woods, 1974). These exclusive preferences were attributed in part to an interaction between the concurrent VI VI schedules and the low rates of responding maintained by high doses of cocaine (Iglauer & Woods, 1974). Low rates were not a problem in the present study because the reinforcement contingency was based on number of responses. MacDonall (1988) also found, in his study of nonindependent concurrent VR VR schedules, that the distribution of responses matched the relative frequency of food-pellet delivery. The one exception was a condition in which 99% of the food pellets were programmed to occur under one schedule.

MacDonall (1988) stated that the nonindependent concurrent VR VR schedules are formally equivalent to concurrent VI VI schedules. However, there are some differences between the two schedules. For example, although the passage of time does contribute to the completion of the concurrent VI VI schedules, the passage of time is neither the contingent response nor the dependent measure (for two exceptions, see Baum & Rachlin, 1969, and Brownstein, 1971). Moreover, with an interval schedule, increases in preference have little influence on reinforcement rate. With the concurrent VR VR schedules, reinforcement rate on the side on which

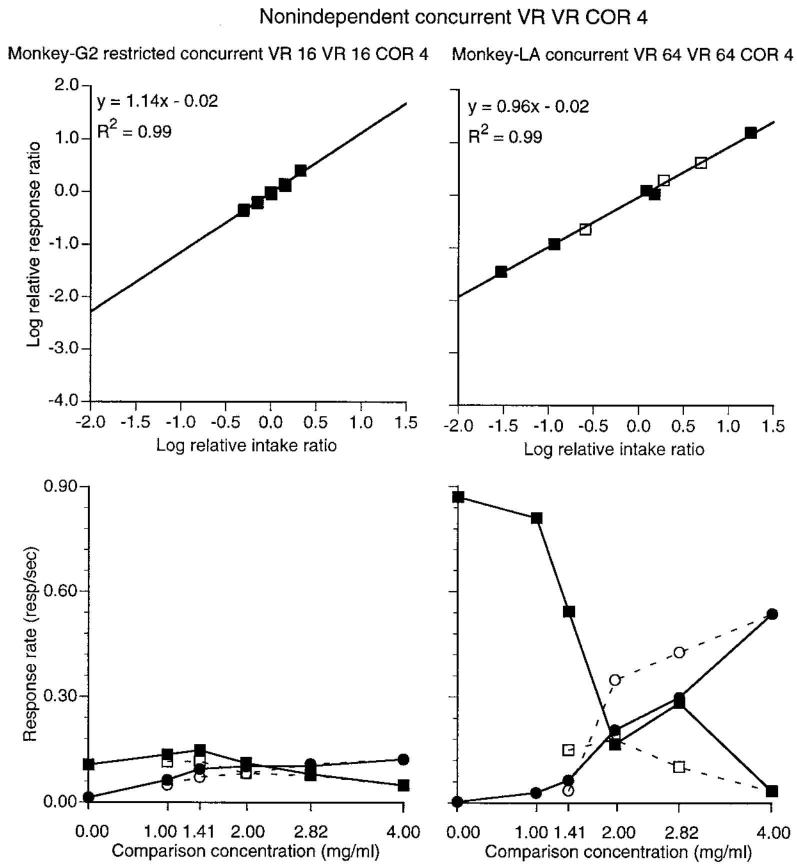

Fig. 3. Performance under the changeover ratio (COR) requirement. Note that Monkey LA responded under a standard concurrent nonindependent schedule, whereas Monkey G2 responded under a restricted concurrent nonindependent schedule. See Appendix C for the standard error of the means (*SEM*). All other details are the same as Figure 1.

the subject responds depends directly on response rate, and this dependence could exaggerate side preferences.

The nonindependent concurrent VR VR schedules can be contrasted with a conventionally arranged concurrent VR VR (or FR FR) schedule. A critical difference between nonindependent schedules and the conventional or independent concurrent VR VR schedules is that under the nonindependent schedules the mean ratio of responses per reinforcer can vary. An extreme example is that under a nonindependent concurrent VR 32 VR 32 schedule, the mean ratio of responses per delivery for one reinforcer could be 32 and the ratio for the other reinforcer could be 1. Such a difference would arise when a subject emitted almost all responses under one schedule such that when the subject switched to the other schedule, one response would be sufficient for the delivery of the reinforcer. That the mean number of responses can vary is an important dimension of nonindependent concurrent schedules, because it permits a finer grained measure of relative reinforcing effects than would occur under conventional concurrent FR FR or VR VR schedules.

A possible interpretation of the present results is that responding occurred on both spouts due to difficulty in discriminating between concentrations. However, in previous studies of oral pentobarbital reinforcement with monkeys, changing the concentration of pentobarbital produced rapid changes in responding (Meisch & Lemaire, 1988; Meisch et al., 1992). Another possible interpretation is that due to the relatively small number of sessions at each point, performance was not asymptotic. However, behavior was stable according to criteria used in previous studies in our laboratory, and the results of these previous studies have been systematically replicated. The smaller number of sessions may be due to the monkeys' extensive histories under similar conditions and also to factors such as the reinforcer, the schedules, and the use of primate subjects.

The sensitivity estimates in our study showed overmatching, whereas most studies report undermatching (Davison & McCarthy, 1988). Overmatching refers to a slope that is greater than 1.00 and indicates that changes in relative reinforcer magnitude correspond with greater changes in relative response rate. The overmatching could be due to the concurrent VR VR schedules or to the pentobarbital reinforcer. Alternatively, overmatching in the present study may be due to manipulation of reinforcer size rather than to the VR schedules. However, the present findings do not permit identification of the responsible variable.

The matching law has been used in drug self-administration studies to assess factors other than changes in dose (Woolverton, 1996). For example, rats' preference for ethanol under concurrent VI VI schedules (Heyman, 1993) and concurrent VR VR schedules (Petry & Heyman, 1995) has been evaluated in relation to the matching law. The results of the present study suggest that the matching law may also apply to the measurement of relative drug reinforcing effects.

Most studies that pertain to the matching law have used time-based schedules. When response rates are low, time-based schedules may not be appropriate. Because matching can occur under nonindependent ratio schedules, these ratio schedules can be used in studies of preference. The present findings extend MacDonall's (1988) results with rats and food reinforcement to nonhuman primates and oral drug reinforcement. The present findings also suggest that the scope of the matching law will be increased by further study of nonindependent ratio schedules.

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APPENDIX A

Nonindependent concurrent VR VR conditions listed in the order in which they were conducted. Also shown are the number of sessions per condition, mean response rate (per second), and mean pentobarbital intake (mg/kg) for each monkey in each of the experimental conditions. In each condition, water or a particular pentobarbital concentration (the comparison concentration) was available concurrently with a standard pentobarbital concentration (2 mg/ml) under a nonindependent concurrent VR 32 VR 32 schedule of pentobarbital reinforcement. Means are for the last six sessions of each condition; numbers in parentheses indicate the *SEM.*

Comparison concentration (mg/ml)	Monkey G2					Monkey LA					Monkey P				
	Number of sessions	Standard		Comparison		Number of sessions	Standard		Comparison		Number of sessions	Standard		Comparison	
		Rate	Intake	Rate	Intake		Rate	Intake	Rate	Intake		Rate	Intake	Rate	Intake
0.00	11	0.47	22.75	0.01		6	0.61	28.79	0.01		6	0.33	16.64	0.00	
		(0.01)		(0.00)			(0.04)		(0.00)			(0.03)		(0.00)	
1.00	8	0.43	21.52	0.03	1.33	8	0.60	28.38	0.01	2.44	7	0.35	18.92	0.01	1.94
		(0.01)		(0.01)			(0.02)		(0.00)			(0.02)		(0.01)	
1.41	7	0.41	20.80	0.05	3.22	17	0.53	26.11	0.04	5.87	12	0.37	19.43	0.02	5.01
		(0.01)		(0.00)			(0.01)		(0.01)			(0.02)		(0.01)	
2.00	9	0.23	14.04	0.20	12.88	13	0.24	16.91	0.20	13.32	20	0.12	11.24	0.16	12.22
		(0.04)		(0.05)			(0.08)		(0.06)			(0.05)		(0.05)	
2.82	8	0.03	3.80	0.33	24.11	7	0.24	15.45	0.26	21.15	6	0.10	11.94	0.20	19.65
		(0.01)		(0.02)			(0.10)		(0.09)			(0.02)		(0.03)	
4.00	6	0.02	1.90	0.31	26.01	7	0.03	4.94	0.37	36.90	9	0.02	6.65	0.26	28.34
		(0.01)		(0.01)			(0.01)		(0.03)			(0.01)		(0.02)	
2.82	8	0.05	3.87	0.31	22.17	9	0.22	15.94	0.28	21.65	12	0.03	8.60	0.30	23.17
		(0.01)		(0.01)			(0.10)		(0.08)			(0.01)		(0.02)	
2.00	9	0.18	11.08	0.19	11.90	16	0.27	17.50	0.30	18.78	9	0.17	14.53	0.17	14.20
		(0.04)		(0.03)			(0.12)		(0.13)			(0.07)		(0.06)	
1.41	6	0.42	21.15	0.03	1.79	6	0.39	21.97	0.12	7.89	6	0.34	18.74	0.04	7.15
		(0.02)		(0.01)			(0.07)		(0.05)			(0.02)		(0.02)	
1.00	6	0.45	22.04	0.01	0.65	11	0.30	17.31	0.19	7.21	11	0.42	22.38	0.02	4.33
		(0.02)		(0.00)			(0.07)		(0.10)			(0.03)		(0.00)	
0.00	9	0.40	19.57	0.00		11	0.55	28.62	0.08		11	0.53	27.38	0.01	
		(0.01)		(0.00)			(0.04)		(0.04)			(0.03)		(0.00)	

APPENDIX B

Restricted nonindependent concurrent VR VR conditions listed in the order in which they were conducted. Also shown are the number of sessions per condition, mean response rate (per second), and mean pentobarbital intake (mg/kg) for each monkey in each of the experimental conditions. In each condition, water or a particular pentobarbital concentration (the comparison concentration) was available concurrently with a standard pentobarbital concentration (2 mg/ml) under a restricted nonindependent concurrent VR 16 VR 16 (Monkey G2) or a concurrent VR 64 VR 64 (Monkey LA) schedule of pentobarbital reinforcement. Means are for the last six sessions of each condition; numbers in parentheses indicate the *SEM*.

Comparison concentration (mg/ml)	Monkey G2					Monkey LA				
	Number of sessions	Standard		Comparison		Number of sessions	Standard		Comparison	
		Rate	Intake	Rate	Intake		Rate	Intake	Rate	Intake
0.00	14	0.17	4.49	0.01		6	0.42	7.90	0.01	
		(0.04)		(0.00)			(0.04)		(0.00)	
1.00	6	0.17	10.78	0.04	5.16	8	0.34	8.34	0.03	3.97
		(0.02)		(0.01)			(0.02)		(0.00)	
1.41	9	0.12	12.07	0.06	8.19	10	0.27	9.04	0.13	6.24
		(0.03)		(0.02)			(0.05)		(0.05)	
2.00	7	0.09	11.45	0.08	11.08	7	0.28	10.68	0.24	10.76
		(0.03)		(0.03)			(0.09)		(0.09)	
2.82	7	0.07	10.29	0.10	14.65	9	0.19	8.91	0.21	12.13
		(0.03)		(0.03)			(0.06)		(0.09)	
4.00	12	0.04	9.48	0.12	19.49	6	0.15	9.09	0.26	18.64
		(0.01)		(0.03)			(0.06)		(0.06)	
2.82	6	0.06	10.96	0.11	16.04	6	0.23	10.19	0.22	14.23
		(0.01)		(0.03)			(0.07)		(0.05)	
2.00	7	0.06	9.13	0.07	9.28	11	0.19	9.81	0.23	9.60
		(0.02)		(0.02)			(0.07)		(0.08)	
1.41	8	0.04	5.50	0.04	3.91	9	0.25	10.81	0.23	7.96
		(0.01)		(0.01)			(0.09)		(0.08)	
1.00	7	0.05	4.29	0.01	2.12	7	0.26	10.22	0.19	5.07
		(0.01)		(0.00)			(0.09)		(0.07)	
0.00	10	0.17	8.14	0.01		7	0.50	11.29	0.03	
		(0.05)		(0.00)			(0.04)		(0.01)	

APPENDIX C

Nonindependent concurrent VR VR conditions with a changeover ratio 4 requirement in effect, listed in the order in which they were conducted. Also shown are the number of sessions per condition, mean response rate (per second), and mean pentobarbital intake (mg/kg) for each monkey in each of the experimental conditions. In each condition, water or a particular pentobarbital concentration (the comparison concentration) was available concurrently with a standard pentobarbital concentration (2 mg/ml) under a restricted nonindependent concurrent VR 16 VR 16 (Monkey G2) or a nonindependent concurrent VR 64 VR 64 (Monkey LA) schedule of pentobarbital reinforcement. Means are for the last six sessions of each condition; numbers in parentheses indicate the *SEM*.

Comparison concentration (mg/ml)	Monkey G2					Monkey LA				
	Number of sessions	Standard		Comparison		Number of sessions	Standard		Comparison	
		Rate	Intake	Rate	Intake		Rate	Intake	Rate	Intake
0.00	9	0.11 (0.03)	3.38	0.01 (0.01)		7	0.87 (0.05)	19.54	0.00 (0.00)	
1.00	6	0.14 (0.01)	9.62	0.06 (0.01)	4.79	11	0.82 (0.06)	18.30	0.03 (0.02)	0.54
1.41	6	0.15 (0.03)	12.68	0.09 (0.02)	8.84	14	0.54 (0.08)	12.02	0.06 (0.02)	1.38
2.00	9	0.11 (0.02)	11.38	0.10 (0.02)	11.45	7	0.17 (0.09)	4.14	0.21 (0.09)	4.94
2.82	6	0.08 (0.02)	9.35	0.10 (0.01)	13.19	6	0.28 (0.14)	6.62	0.30 (0.10)	9.77
4.00	7	0.05 (0.01)	7.63	0.12 (0.01)	16.14	10	0.03 (0.02)	1.47	0.54 (0.02)	25.21
2.82	12	0.08 (0.01)	10.32	0.11 (0.02)	14.58	7	0.10 (0.02)	2.91	0.43 (0.08)	14.07
2.00	8	0.08 (0.01)	9.48	0.08 (0.01)	9.35	11	0.18 (0.10)	4.52	0.35 (0.12)	8.44
1.41	8	0.12 (0.02)	9.99	0.07 (0.01)	6.98	7	0.15 (0.07)	3.48	0.04 (0.01)	0.88
1.00	11	0.12 (0.02)	8.32	0.05 (0.01)	4.11					
0.00										